PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

09 JUL 2004

Applicant's or agent's file reference 43952/JMD/MR	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/00078	International filing date *(day/month/year)* 10.01.2003	Priority date *(day/month/year)* 10.01.2002
International Patent Classification (IPC) or both national classification and IPC C12N15/62		
Applicant UNIVERSITY OF NEWCASTLE UPON TYNE et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08.08.2003	23.04.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Surdej, P Telephone No. +49 89 2399-7334

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/00078

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-27 as originally filed

Claims, Numbers

1-36 as originally filed

Drawings, Sheets

1/9-9/9 as originally filed

Sequence listing part of the description, pages:

1-26, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4-7,9-11,13,15,20-21,25,33-34
	No:	Claims	1-3, 8, 12, 14, 16-19, 22-24, 26-32, 35-36
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-36
Industrial applicability (IA)	Yes:	Claims	1-36
	No:	Claims	

2. Citations and explanations

   see separate sheet

Reference is made to the following documents:

D1: RIECHMANN LUTZ ET AL: 'The C-terminal domain of TolA is the coreceptor for filamentous phage infection of E. coli.' CELL, vol. 90, no. 2, 1997, pages 351-360

D2: WO 01 21817 A (MUYLDERMANS SERGE ;VLAAMS INTERUNIVERSITAIR INST (BE); SILENCE KAR) 29 March 2001 (2001-03-29)

D3: LUBKOWSKI JACEK ET AL: 'Filamentous phage infection: Crystal structure of g3p in complex with its coreceptor, the C-terminal domain of TolA.' STRUCTURE (LONDON), vol. 7, no. 6, June 1999 (1999-06), pages 711-722

D4: DEROUICHE RAHMONA ET AL: 'Binding of colicins A and E1 to purified TolA domains.' MICROBIOLOGY (READING), vol. 143, no. 10, 1997, pages 3185-3192

D5: WAN ET AL: 'TolAIII co-overexpression facilitates the recovery of periplasmic recombinant proteins into the growth medium of Escherichia coli' PROTEIN EXPRESSION AND PURIFICATION, ACADEMIC PRESS, US, vol. 14, no. 1, October 1998 (1998-10), pages 13-22

D6: EP-A-0 299 810 (INST NAT SANTE RECH MED ;CENTRE NAT RECH SCIENT (FR); PASTEUR INST) 18 January 1989 (1989-01-18)

D7: LAVALLIE E R ET AL: 'A THIOREDOXIN GENE FUSION EXPRESSION SYSTEM THAT CIRCUMVENTS INCLUSION BODY FORMATION IN THE E. COLI CYTOPLASM' BIO/TECHNOLOGY, NATURE PUBLISHING CO. NEW YORK, US, vol. 11, no. 2, February 1993 (1993-02), pages 187-193

D8: DEPREZ CHRISTOPHE ET AL: 'Macromolecular import into Escherichia coli: the TolA C-terminal domain changes conformation when interacting with the colicin A toxin.' BIOCHEMISTRY. UNITED STATES 26 FEB 2002, vol. 41, no. 8, 26 February 2002 (2002-02-26), pages 2589-2598

D9: WALBURGER ANNE ET AL: 'The Tol/Pal system function requires an interaction between the C-terminal domain of TolA and the N-terminal domain of TolB.' MOLECULAR MICROBIOLOGY, vol. 44, no. 3, May 2002 (2002-05), pages 695-708

Introduction

The application discloses a fusion polypeptide comprising a TolAIII domain fused to a non tolA polypeptide and uses thereof.

1. Not all the priority documents were available at the time of the establishment of the International Preliminary Examination Report (IPER) which consequently has been established assuming that all the claims are entitled to the earliest claimed priority. Should, however, the priority be invalid, the Applicant is informed that documents D9 would be detrimental to the novelty and/or inventivity of the claimed subject-matter.

Re Item V

Reasoned statement under Article 35(2) PCT with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty and inventive step (Art. 33(1)-(3) PCT)

2. Claims 1-3, 8, 12, 14, 16-19, 22-24, 26-32, 35-36 are not new in view of D2 and/or D1. D2 discloses a fusion polypeptide for expression in a host cell comprising a TolAIII domain and a non-TolA polypeptide, wherein the TolAIII domain is located towards the N-terminus of the fusion polypeptide and the non-TolA polypeptide is located towards the C-terminus of the fusion polypeptide (e.g. page 7, line 26 to page 8, line 8). D2 discloses methods to produce said fusion polypeptide, use of said fusion polypeptide to isolate or to study the interaction property of the non-TolA polypeptide (e.g. page 7-8). D1 discloses a construct having tolAIII domain linked to a C-terminal His tag (e.g. page 353, left column, page 358, right column).

3. The claimed subject-matter of claims 4-7, 9-11, 13, 15, 20, 25, 33-34 is not inventive in the light of D1 or D2 in combination with either D3-D5, D7. The features of said claims are merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed. It should be also noted that changing the position of the TolA and non-TolA parts is an obvious alternative.